

# Smallpox

Report Immediately

October 2003

## 1) THE DISEASE AND ITS EPIDEMIOLOGY

### A. Etiologic Agent

Smallpox is caused by the variola virus, which belongs to the genus orthopoxvirus.

### B. Clinical Description and Laboratory Diagnosis

Smallpox is a systemic viral disease, which presents with a characteristic eruptive rash. The onset of smallpox is sudden, with a prodrome characterized by fever, malaise, headache, severe backache, prostration, and occasionally abdominal pain. After 2-4 days the temperature falls and a rash appears.

The rash progresses through successive stages of macules, papules, vesicles, pustules, and finally scabs that fall off at the end of the 3<sup>rd</sup> – 4<sup>th</sup> week of illness; the lesions are at the same stage of development in any given area. The fever frequently rises as the rash progresses to the pustular stage. The lesions first appear on the face and subsequently on the body and extremities, are more abundant on the face and extremities than on the trunk (centrifugal distribution), and are abundant over prominences and extensor surfaces. In previously vaccinated persons, the illness may be significantly modified to the extent that systemic symptoms are absent to mild and the rash consists of only a few highly atypical lesions, which do not pass through the usual successive stages.

Two principal clinical-epidemiologic varieties of smallpox are recognized: variola minor (alastrim) with a case-fatality ratio of less than 1%, and variola major (classical smallpox) with a case-fatality ratio among the unvaccinated of 15 – 40%. Death occurs as early as the 3<sup>rd</sup> – 4<sup>th</sup> day of development of rash but more usually during the 2<sup>nd</sup> week. Approximately 3% of hospitalized variola major cases experience a fulminating disease characterized by a severe prodrome, prostration and bleeding into the skin and mucous membranes, uterus and genital tract, especially in pregnant women; such hemorrhagic cases are rapidly fatal. In some instances when the usual rash does not appear, disease was confused with severe acute leukemia, meningococcemia or idiopathic thrombocytopenic purpura.

In the highly lethal “flat” variety, observed in about 5% of cases, the focal lesions are slow to develop, and the vesicles contain very little fluid and tend to project only slightly above the surrounding skin and are soft and velvety to the touch. In the few patients with this type who survived, the lesions sometimes resolve without the usual pustulation and crusting.

Variola minor is associated with the rash similar to that observed in variola major; however, the patient generally experiences less severe systemic reactions. Smallpox is usually distinguished by the clear-cut prodromal illness, the centrifugal distribution of the rash, the appearance of all lesions more or less simultaneously, the similarity in appearance of all lesions in a given area, and its more deeply seated lesions.

The disease most commonly confused with smallpox is chickenpox.

	Smallpox (Variola): clinical features	Chickenpox (Varicella): clinical features
<b>Major distinguishing features</b>	<ul style="list-style-type: none"> <li>• Febrile prodrome: temperature &gt;102 and systemic symptoms (prostration, severe headache, backache, abdominal pain, or vomiting) 1-4 days <i>before</i> rash onset</li> </ul>	<ul style="list-style-type: none"> <li>• No or mild prodrome before rash onset</li> </ul>
	<ul style="list-style-type: none"> <li>• Lesions are deep, firm, well-circumscribed pustules; may be confluent or umbilicated</li> </ul>	<ul style="list-style-type: none"> <li>• Lesions typically superficial vesicles</li> </ul>
<b>Other distinguishing features</b>	<ul style="list-style-type: none"> <li>• Rash concentrated on face and distal extremities (centrifugal)</li> </ul>	<ul style="list-style-type: none"> <li>• Rash concentrated on trunk and proximal extremities (+/- face, scalp)</li> </ul>
	<ul style="list-style-type: none"> <li>• Rash in same stage of evolution on any one part of the body</li> </ul>	<ul style="list-style-type: none"> <li>• Rash appears in crops so lesions are in different stages of evolution (papules, vesicles, crusts) on any one part of the body</li> </ul>
	<ul style="list-style-type: none"> <li>• First lesions on oral mucosa/palate (enanthem); followed by examthem (rash) on face or forearm</li> </ul>	<ul style="list-style-type: none"> <li>• First lesions on trunk (occasionally face)</li> </ul>
	<ul style="list-style-type: none"> <li>• Lesions on palms and soles (seen in &gt; 50%)</li> </ul>	<ul style="list-style-type: none"> <li>• Lesions very uncommon on palms and soles</li> </ul>
	<ul style="list-style-type: none"> <li>• Lesions may itch at scabbing stage</li> </ul>	<ul style="list-style-type: none"> <li>• Lesions generally intensely itchy</li> </ul>
	<ul style="list-style-type: none"> <li>• Lesions evolve from papule→pustule in days</li> </ul>	<ul style="list-style-type: none"> <li>• Lesions generally evolve from macules to papules to vesicles to crusts in &lt;24 hours</li> </ul>
	<ul style="list-style-type: none"> <li>• Illness lasts 14 to 21 days</li> </ul>	<ul style="list-style-type: none"> <li>• Illness lasts 4-7 days</li> </ul>

Laboratory diagnosis is based on identification of virus by direct electron microscopy, immunohistochemistry, and polymerase chain reaction (PCR). Isolation of virus on live-cell cultures, followed by nucleic acid identification, or growth on chorioallantois, is confirmatory. The serologic testing does not differentiate among orthopoxvirus species, and paired serum samples are required to distinguish recent infection from vaccination in the remote past. **Testing specifically for variola can be performed at Level C or D laboratories only.**

### C. Reservoirs

Prior to eradication, man was the only reservoir; now the only known virus is held in two secured laboratories.

### D. Modes of Transmission

Smallpox is spread by close contact with respiratory discharges and skin lesions of patients, or material, which infected persons had recently contaminated; airborne spread of variola is infrequent.

Household, hospital and school contacts are especially at risk.

Spread to laundry workers by contaminated bedding and other linens has been frequently observed.

Inapparent infections have not been implicated, but unrecognized cases sometimes lead to extensive secondary spread. The secondary attack rate among unvaccinated populations is approximately 58% (range 38-88% in eight studies).

### E. Incubation Period

The incubation period for smallpox is 7 – 19 days, commonly 10 – 14 days to onset of illness and 2 – 4 days more to onset of rash.

## F. Period of Communicability or Infectious Period

Smallpox patients are generally not infectious to others until the onset of rash (approximately 7-17 days after exposure). However since the exact date of rash onset may not be noted accurately and because of the infectious enanthem (lesions in the mouth and the posterior pharynx), which may precede cutaneous rash onset by 1-2 days, **case-patients should be considered potentially infectious from the date of onset of fever.** The period of highest transmission is during the first 7-10 days after onset of rash. However, a person is considered infectious until all scabs have separated. Risk of contracting disease increases during winter and early spring, because aerosolized orthopoxviruses survive longer at lower temperatures and low levels of humidity.

## G. Epidemiology

Smallpox was declared eradicated by the World Health Organization in 1979. The last known naturally occurring case was in 1977. In 1980 the World Health Assembly announced that smallpox had been eradicated and recommended that all countries cease vaccination. The last remaining samples of smallpox virus officially reside in two places: the Centers for Disease Control and Prevention in the United States and the Research Institute for Viral Preparations in Moscow.

## I. Bioterrorist Potential

Smallpox, because of its high case-fatality ratios and transmissibility, now represents one of the most serious bioterrorist threats to the civilian population.

Introduction of variola virus into a nonimmune population could result in a major disaster unless controlled promptly.

There is speculation that smallpox may have been obtained by rogue nations from the Soviets, or that Soviet scientists may have sought work with rogue nations developing biological weaponry.

# 2) REPORTING CRITERIA AND LABORATORY TESTING SERVICES

## A. New Jersey Department of Health and Senior Services (NJDHSS) Case Definition

### CASE CLASSIFICATION

#### A. CONFIRMED

A clinically compatible illness, **AND**

- Isolation of smallpox (variola) virus from a clinical specimen (Level D\* laboratory only), **OR**
- Polymerase chain reaction (PCR) identification of variola DNA in a clinical specimen (Level D\* laboratory only), **OR**
- Negative stain electron microscopy (EM) identification of variola virus in a clinical specimen (Level D\* laboratory or approved Level C\*\* laboratory).

\* CDC and USAMRIID

\*\* The NJ Public Health and Environmental Laboratories, NJDHSS, and others that have required safety and containment facilities.

#### B. PROBABLE

A clinically compatible illness that is not laboratory confirmed, but has an epidemiological link to another confirmed or probable case.

### C. POSSIBLE

- A clinically compatible illness that is not laboratory confirmed and does not have an epidemiological link to a confirmed or probable case of smallpox, **OR**
- A case that has an atypical presentation that is not laboratory confirmed but has an epidemiological link to a confirmed or probable case of smallpox. Atypical presentations of smallpox include (a) hemorrhagic lesions or (b) flat, velvety lesions not appearing as typical vesicles nor progressing to pustules.

#### NOTE:

1. The case definitions above (which are identical to CDC's) may require revision by public health personnel conducting the epidemiological investigation depending upon the specifics of the epidemic.
2. **Report any suspicion of smallpox called to your attention by a healthcare provider or any positive laboratory result pertaining to smallpox.**
3. **Report any other communications regarding smallpox received from anonymous sources.**

Initial confirmation of a smallpox outbreak requires testing in a Level D laboratory (CDC and USAMRIID). Level C laboratories (e.g., NJPHEL) will assist with testing of clinical specimens following initial confirmation of an outbreak by CDC.

### B. Laboratory Testing Services Available

The Public Health and Environmental Laboratory (PHEL) does not provide testing for variola virus. However, other tests can be run to rule out other illnesses with similar clinical features (See attached "List of available at PHEL tests when investigating possible smallpox case").

Specimens can be sent to PHEL for referral to a BSL4 facility after evaluation by the Bioterrorism Unit of the IZDP Program at 609.588.7500. Procedures for submitting specimens for suspected cases of smallpox may also be found on the Centers for Disease Control and Prevention website at CDC <http://www.cdc.gov/bt>.

## 3) DISEASE REPORTING AND CASE INVESTIGATION

### A. Purpose of Surveillance, Reporting and Case Investigations

1. To identify potential sources of transmission in the United States, and to stop transmission from such sources.
2. To identify sources of transmission and geographical areas of risk outside the United States and to stop transmission from such sources.
3. To identify cases as early as possible, establish the diagnosis and case classification, and prevent transmission to other persons.
4. To identify cases and clusters of human illness that may be associated with a bioterrorist event.
5. To identify contacts for tracing, vaccination and surveillance.
6. To impose isolation of confirmed, probable and suspected cases.
7. To monitor the clinical course and outcome of cases.
8. To monitor the epidemiology of the outbreak for analysis and communications purposes.

### B. Laboratory and Healthcare Provider Reporting Requirements

Any case of smallpox is considered an **INTERNATIONAL EMERGENCY**. The NJDHSS requests that information about any suspect or known case of smallpox be **immediately reported** to the local health officer where diagnosed. If this is not possible, call the NJDHSS Infectious and Zoonotic Disease Program (IZDP) at 609.588.7500 (business hours), or 609.392.2020 (emergency number for nights/weekends).

## C. Local Department of Health Responsibilities

### 1. Reporting Requirements

The New Jersey Administrative Code (N.J.A.C. 8:57-1.8) stipulates that each local health officer must report any case of smallpox (as defined by the reporting criteria in Section 2A above) immediately to NJDHSS IZDP at 609.588.7500 (business hours), or 609. 392.2020 (emergency number for nights/weekends).

### 2. Case Investigation

- a. **The most important step a local health officer can take if he/she learns of a suspect or confirmed case of smallpox, or potential exposure to smallpox, is to call the NJDHSS Infectious and Zoonotic Disease Program, any time of the day or night.** The daytime phone number is 609.588.7500. The emergency phone number for nights and weekends is 609.392.2020.
- b. The NJDHSS Infectious and Zoonotic Disease Program will direct case investigations of smallpox in New Jersey residents in conjunction with CDC and other state and federal agencies. A confirmed case of smallpox will indicate a bioterrorist event until proven otherwise since naturally occurring variola was eradicated in 1977. The FBI and other response authorities will be involved, and the investigation will be done in close cooperation with the local health officer. Laboratory confirmation is important for a first case in a geographic area, leading to release of vaccine as part of a response. In a setting where multiple cases are identified, laboratory capacity may soon be overwhelmed. In such instances, priority for laboratory resources will include (1) testing of clinical or environmental specimens that will provide information about a potential source of exposure, facilitating law enforcement activities and case detection; and (2) testing of clinical specimens from cases with an unclear presentation but who are suspected as cases following expert consultation.
- c. **Following** immediate notification of the NJDHSS, the local health officer may be asked to assist in investigating cases that live within his/her jurisdiction, including gathering the following:
  - 1) The patient's name, age, date of birth, address, phone number, race, ethnicity, status (hospitalized, at home, deceased), medical conditions that are risk factors for severe disease and outcome, and parent/guardian information, if applicable.
  - 2) The name and phone number of the hospital where the case-patient is or was hospitalized.
  - 3) The name and phone number of the case-patient's attending physician if hospitalized.
  - 4) The name and phone number of the infection control professional at the hospital if hospitalized.
  - 5) If the patient was seen by a healthcare provider before hospitalization, or seen at more than one hospital, be sure to document these names and phone numbers as well.
- d. The local health officer may be asked to assist in the epidemiologic investigation using a [CDS-1](#) form or the report can be filed electronically over the Internet using the confidential and secure Communicable Disease Reporting System (CDRS). Most of the information can be obtained from the provider or the medical record. Use the following guidelines in completing the report:
  - 1) Accurately record demographic information.
  - 2) Record a description of the patient's presentation (i.e., type of rash).
  - 3) Be sure to record date and time of the onset of illness, symptom information, date and time of the onset of the rash, patient status (e.g., recovered, died) accurately.
  - 4) Exposure history: Is there a known exposure to a confirmed case? If not, use the longest incubation period for smallpox (7 to 21 days). Specifically, focus on the period beginning a minimum of 1 day prior to the case's onset date back to no more than 30 days before onset for the following exposures:
    - a) Travel history: determine the date(s) and geographic area(s) traveled to by the case-patient to identify where the patient may have become infected.

- b) Exposure to known case-patient: determine contact with known patients or individuals with rash presentations.
  - c) Laboratory exposure: determine whether the case-patient works in a laboratory.
- 5) If there have been several attempts to obtain patient information (*e.g.*, the patient or healthcare provider does not return calls, or the case refuses to divulge information or is too ill to be interviewed), please obtain as much information as possible. Please note on the report the reason why it could not be filled out completely. **If CDRS is used to report, enter the collected information regarding exposure history, travel and any additional information into the “Comments” section.**
- 6) After completing the form, attach lab report(s) and fax to the NJDHSS Infectious and Zoonotic Diseases Program. The fax number is 609.631.4863. The report can be filed electronically over the Internet using the confidential and secure CDRS. Call the IZDP to confirm receipt of your fax.
- e. **Contact identification** is the most urgent task when investigating smallpox cases. A contact is defined as a person who has had contact with a suspected, probable or confirmed case of smallpox. A contact’s risk of contracting smallpox increases with close contact (6 feet or less), increasing length of exposure to a case-patient and the stage and severity of the case-patient’s illness (*i.e.*, contact’s risk depend on case-patient’s onset of rash and/or cough). Thus, close contact is defined as any face-to-face contact ( $\leq 6$  feet, able to reach out and touch) with a smallpox case-patient. Duration of contact should be quantified, if possible. Vaccinate close contacts as soon as possible following exposure, but preferably within 3 – 4 days to prevent or modify disease. This was the successful strategy used for the global eradication of smallpox.
- f. Institution of disease control measures is an integral part of case investigation. It is the local health officer’s responsibility to understand, and, if necessary, institute in conjunction with NJDHSS and CDC the control guidelines listed below in Section 4, “Controlling Further Spread.”

## 4) CONTROLLING FURTHER SPREAD

### A. Isolation and Quarantine Requirements

#### 1. Minimum Period of Isolation of Patient

- a. Strict isolation precautions until all scabs have separated.

**NOTE:** Infection can be transmitted by air currents, and virus can be carried on by various materials contaminated by the patient, especially on clothing and linen.

#### 2. Minimum Period of Quarantine of Contacts

- a. All persons living in the same house with the smallpox patient, as well as face-to-face contacts should be vaccinated promptly with known potent vaccine and placed under daily surveillance for 21 days after last contact with the smallpox patient.
- b. Quarantine should be substituted for surveillance of intimate contacts whose cooperation is uncertain.
- c. At the first sign of fever or other illness, the individual should be isolated.
- d. Any intimate contact who has not been vaccinated (as determined by the absence of a vaccination scar) and who refuses vaccination should be placed under quarantine for the period when disease might appear, *i.e.*, from 7 days after the first contact to 19 days after the last exposure to a case.

## B. Protection of Contacts of a Case

1. While a patient is being transported from the emergency department or clinic to an in-patient room, the patient should wear a surgical mask. A sheet should be used to cover the skin as much as possible and efforts should be made to limit patient movement and manipulations of the linen, to minimize aerosolization.
2. Minimize the number of persons who enter the patient's room, as well as the traffic in and out of the room, as much as possible. All hospital staff (including transport personnel) and visitors (limited to immediate family ONLY) must don contact and airborne personal protection equipment prior to entering a suspected or confirmed smallpox patient's room (i.e., disposable gloves, gowns and a surgical mask or properly fit-tested respirator, N-95 or higher; see NJ Smallpox Vaccination Plan, section II D1B, pages 28-29, for more information).
  - a. Preferably, no staff without at least one prior vaccination for smallpox should be allowed in the patient's room.
  - b. Ensure that all staff and visitors entering the room are instructed in the meaning of contact and airborne precautions.
  - c. Dedicated equipment (e.g., blood pressure cuffs and stethoscopes) should be left in the room when possible. No personal equipment (e.g., stethoscopes) should be used on the suspect patient and then taken out of the room for use on other patients until decontaminated. A disinfectant labeled "tuberculocidal" is recommended for use on diagnostic equipment used on the patient.
  - d. Use disposable items whenever possible. Arrange to have food brought into the room in disposable containers. Disinfect and/or sterilize non-disposable medical devices according to the manufacturer's specifications. **No extraordinary efforts are necessary.** Articles contaminated with excessive blood or body fluids (i.e., lesions or respiratory secretions) should be handled as regulated medical waste. All other non-sharps waste can be handled as regular waste.
  - e. Ideally all laundry and linens (e.g., bedding, towels) should be handled by the vaccinated staff caring for the patient. Laundry/linen can be put in impervious bags in the patient's room. Any staff wearing gloves can transport the bagged linen according to the hospital's standard laundry protocol.
3. Immunization of contacts:
  - a. All contacts of a laboratory-confirmed smallpox case, both intimate and casual, should be promptly vaccinated, employing a known potent vaccine. Epidemiological studies have shown that an increased level of protection against smallpox persists for  $\leq 5$  years after primary vaccination and substantial but waning immunity can persist for  $\geq 10$  years. Antibody levels after revaccination can remain high for a longer period, conferring a greater period of immunity than occurs after primary vaccination alone. Although it is assumed that adults  $>30$  years of age in the United States have little or no immunity to smallpox, there is evidence that vaccination during infancy results in long term reduction in mortality.
4. NJDHSS will immediately obtain assistance from national and international authorities for detailed investigation and for implementation of necessary control measures.
  - a. Vaccine will be made available from national stockpiles or the WHO emergency reserve.
  - b. The number to be vaccinated will depend on the specific circumstances surrounding the event, but in past outbreaks, vaccination of a few hundred to a few thousand persons has successfully stopped spread. The local health department will be responsible for making vaccination clinics available, with coordination accountability at the LINCIS site.
  - c. At this time, when there is no known smallpox illness, mass vaccination of entire communities considered neither necessary nor desirable to control an outbreak.
5. Investigation of contacts and source of infection:
  - a. Prompt investigation to determine the source of infection is of the greatest importance.
  - b. The diagnosis in some outbreaks was not made until the 3<sup>rd</sup>-4<sup>th</sup> generation of cases.
  - c. Since inapparent cases of smallpox are rare and do not appear to transmit infection, the chain of infection can almost always be determined.
  - d. Persons with supposed "chickenpox" or those who have recently experienced pustular or hemorrhagic disease (especially fatal cases) should be considered as possible sources of infection.

### **C. Managing Special Situations**

One suspected case of smallpox is considered an INTERNATIONAL EMERGENCY.

Therefore NJDHSS and other response authorities will work closely with local boards of health to provide instructions/information on how to proceed.

## **ADDITIONAL INFORMATION**

Technical information about smallpox is available from the Centers for Disease Control and Prevention at [www.bt.cdc.gov/Agent/Smallpox](http://www.bt.cdc.gov/Agent/Smallpox)

The formal CDC surveillance case definition for smallpox is the same as the criteria outlined in Section 2 A of this chapter. CDC case definitions are used by state health departments and CDC to maintain uniform standards for national reporting. For reporting to the NJDHSS, always use the criteria outlined in Section 2 A.

## **REFERENCES**

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